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Short communication

Altered premotor cortical oscillations during repetitive movement in persons with Parkinson's disease

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HIGHLIGHTS

- Motor cortical oscillations recorded over the PMd are suppressed in persons with PD.
- Motor cortical oscillations recorded over the SMA were similar between groups.
- Changes in premotor cortical oscillations may impact repetitive movement.

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ABSTRACT

Premotor areas play a critical role in the control of repetitive movements. While research has shown that movement-related oscillations are abnormal during repetitive movements in persons with Parkinson's disease (PD), there is limited research examining the contribution of premotor areas, such as the contralateral dorsal premotor area (PMd) and supplementary motor area (SMA), to this impairment. This study compared movement-related oscillations over premotor regions between participants with PD and control participants. Nine participants with PD off and on medication and nine matched control participants were studied. Participants performed cued index finger movements. Spectral power was derived from electroencephalographic recordings from electrodes FC3/FC4 and Cz over the regions of the contralateral PMd and SMA respectively. Movement-related alpha and beta band oscillations were suppressed over electrode FC3/FC4 (contralateral PMd) in participants with PD, particularly at higher movement rates, in both the off and on medication conditions compared to control subjects. The pattern of movement-related oscillations recorded from Cz (SMA) was similar between PD and control groups. This would suggest that the region of the contralateral PMd may be preferentially involved with the control of externally cued repetitive movements and that changes in this activity may contribute to the deterioration of repetitive finger movements at higher rates in persons with PD.

Repetitive movements in people with Parkinson's disease (PD) are characterized by reductions in amplitude (hypokinesia), speed (bradykinesia) and rhythmicity and are frequently accompanied by involuntary hesitations and arrests. The incidence and severity of these impairments increases during small amplitude and/or higher rate movements [1–3]. Moreover, hypokinesia, hesitations and arrest of movement that occur at higher movement rates respond poorly to dopamine replacement therapy [2,3] and are not improved with external cueing [2,4]. Currently, the cortical mechanisms contributing to impaired repetitive movement in PD are poorly understood.

Motor cortical areas considered to be critically involved in the control of finger movements include the primary motor cortex (M1), dorsal premotor area (PMd), and supplementary motor area (SMA) [5–7]. The PMd is thought to be preferentially activated during externally cued movements whereas the SMA is considered to be important for the control of self-paced (internally generated) movements [8–10]. Functional neuroimaging studies of discrete

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movements have shown that internally generated movements in people with PD are associated with reduced activity in the SMA and increased activity in the PMd and M1 [11–14]. Motor and premotor cortical activity during externally paced movements is dependent upon movement rate with activity in the contralateral M1 and PMd increasing with increased rate [6,7]. Findings in the SMA have been equivocal, some studies showing no change in activity with increased rate of movement cueing [5,7] and others showing an increase [6]. Since externally paced movements often deteriorate more at higher movement rates in people with PD [2] and are associated with abnormally suppressed alpha and beta oscillations in M1 [15], this raises the possibility that impaired function of the PMd may contribute to this impairment.

The purpose of this study was to use scalp surface electroencephalography (EEG) to examine movement-related oscillations over the regions of the contralateral PMd and SMA in people with PD and matched control subjects across a range of externally paced movement rates (1–3 Hz). Given that movement was externally cued, we hypothesized that compared to control subjects (1) movement-related oscillations over the regions of the PMd of participants with PD would be suppressed and show impaired scaling with movement rate and (2) there would be no differences in movement-related oscillations over the SMA.

Methods for this study, including more detailed information about participants, have been described in detail in a previous publication [15] and are summarized below.

Participants with a diagnosis of idiopathic PD (n = 9; age = 65 ± 8 years) and age, gender and handedness matched control participants (n = 9; age = 65 ± 9 years) were tested on and off medication. The Institutional Review Board of Northwestern University approved the procedures. All participants gave their written informed consent according to the Declaration of Helsinki.

Each trial began with period of rest (REST). A series of acoustic tones was then presented at a pacing rate of 1 Hz and maintained for 15 intervals. The rate of the tone was then increased by 0.25 Hz until reaching 3.0 Hz [2,15,16]. All participants were asked to synchronize finger-flexion with the tones (MOVE). Participants with PD performed the task with their most affected hand, and control participants performed the task with the same side as their matched counterpart.

An accelerometer (Measurement Specialties EGAXT3-15-/L2M) placed on the index finger was used to capture finger kinematics. Bipolar surface electromyography (EMG) signals were recorded from the first dorsal interosseous (FDI) muscle (Grass P511, Grass Technologies). EEG signals were recorded from a montage of 74 scalp-surface electrodes conformed to the international 10–20 system with increased density of electrodes over the right and left sensorimotor areas (Neuroscan Syamps System/Neuroscan 4.1) [15].

Analysis of event-related power was focused on signals obtained from electrodes FC3 or FC4 (overlying the region of the PMd) contralateral to the moving hand, and electrode Cz (overlying the region of the SMA). A 5-point Laplacian spatial filter was applied to minimize signals common to adjacent electrodes (e.g. C3 and FC3). EEG data were epoched according to movement onset which was manually marked using the EMG and acceleration signals. Epoched data was filtered and inspected for noise accordingly [15]. Movement onset times were superimposed on REST data and MOVE data was then normalized to the REST [17]. Epochs were then averaged across each pacing rate (1–3 Hz) and task condition (REST, MOVE).

A short-time Fourier transform method was used to obtain within-subject time-frequency power spectra profiles [18]. Analysis was focused on the alpha (9–14 Hz) and beta (20–25 Hz) bands as previous research has shown that synchronization – desynchronization transition is greatest within these bands [17]. To obtain time-power plots, normalized power in each frequency band was averaged for each group. The amplitude of movement-related oscillations was derived from measures of the peak-to-peak oscillations observed in the grand average waveform. Area under the curve was calculated at each pacing rate and averaged across groups to capture the overall magnitude of synchronization and desynchronization of movement related oscillations (MROs) across a movement cycle relative to rest.

Analysis was completed to determine if differences in power at REST contributed to power during the MOVE condition. The REST condition was epoched into 1-s segments, and a fast Fourier transform was applied to each segment. The power spectrum was normalized to 1 and summed resulting in a chi-square distribution. The mean spectrum of one group was divided by the mean spectrum of the second group. From the resulting F distribution, statistical comparison of spectrum between groups was completed by obtaining the 95th percentile confidence limits from an F table. Any value below or above these limits was designated a significant difference between spectrums [19].

To test the main hypotheses, a non-parametric Mann-Whitney-U test was used due to the non-Gaussian distribution of the MRO measures, to examine differences in peak-to-peak amplitude and area under the curve between the PD and control groups. The Wilcoxon test was used to test for differences between the PD_{OFF} and PD_{ON} groups and across tone rates. Statistical analysis was completed using SPSS and the level of significance for all tests was set at $\alpha < 0.05$.

Results of analysis of the kinematic data have been published previously [15]. Participants with PD showed an increase in hypokinesia and hastening at pacing rates ranging from 1.75 to 3 Hz both OFF and ON medication compared to the control participants.

Fig. 1 shows the difference in relative power in electrodes FC3/FC4 and Cz recorded over the regions of the contralateral PMd and SMA respectively at rest between the PD and control groups. Fig. 1C and D shows the ratio of the mean spectra between groups in which a peak above or below the 95th lower confidence limit (dashed lines) indicates significance. The participants with PD showed a significant increase in relative power in the alpha band (~9–14 Hz) and suppression in the beta band (~13–30 Hz) in both medication states compared to controls for both electrodes FC3/FC4 (Fig. 1C) and Cz (Fig. 1D).

A visual depiction of the average time-frequency power spectra across all tone rates from electrode FC3/FC4 is shown in Fig. 2. The control group showed a progressive increase in power (more red) in both the alpha and beta bands with increasing movement rate. In contrast, both PD groups showed an attenuation of power in both bands across all tone rates.

Time-frequency plots for the frequencies of interest (9–14 Hz and 20–25 Hz) are shown in Fig. 3. Statistical analysis of peak-to-peak amplitude (peak within the grey shaded region) revealed significant differences between groups. The PD group and controls significantly differed in the alpha and beta bands in both the off and on medication states (PD_{OFF} vs. Control: $Z(1) < -2.427$, $p < 0.015$; PD_{ON} vs. Control: $Z(1) < -3.804$, $p < 0.001$). A significant medication effect (PD_{OFF} vs PD_{ON}) was also revealed for both bands ($Z(1) < -2.312$, $p < 0.021$). For area under the curve, significant main effects of group were observed for alpha band oscillations in both the off and on medication states (PD_{OFF} vs. Control: $Z(1) = -3.706$, $p < 0.001$; PD_{ON} vs. Control: $Z(1) = -2.281$, $p = 0.023$), but not in the beta band. In contrast, there was a significant effect of medication in the beta band ($Z(1) = -2.957$, $p = 0.003$), but not the alpha band.

A visual depiction of the average time-frequency power spectra across all tone rates from electrode Cz is shown in Fig. 4. In both control subjects and participants with PD in the on medication state, MROs at lower (1.0–1.5 Hz) and higher (2.5–3 Hz) tone rates were associated with a distinct suppression of power in the beta range of 20–25 Hz. The pattern was different at tone rates of 1.75–2.25 Hz,